



**TRANSMITTED BY FACSIMILE**

Michelle Sharp  
Director, U.S. Regulatory Affairs  
Eli Lilly and Company  
Lilly Technology Center  
Indianapolis, IN 46221

**RE: NDA #21-427, 21-733, 22-148 Cymbalta (duloxetine hydrochloride) Delayed-Release Capsules for Oral Use  
NDA #20-815, 22-042 EVISTA (raloxifene hydrochloride) Tablets for Oral Use  
NDA #20-509 Gemzar® (gemcitabine HCl) for Injection  
MACMIS ID #17320**

Dear Ms. Sharp:

As part of its monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed Eli Lilly and Company's (Lilly) sponsored links on internet search engines (e.g., Google.com) for the following products: Cymbalta (duloxetine hydrochloride) Delayed-Release Capsules (Cymbalta), EVISTA (raloxifene hydrochloride) Tablets (Evista), and Gemzar (gemcitabine HCl) for Injection (Gemzar). The sponsored links cited in this letter are misleading because they make representations and/or suggestions about the efficacy of Cymbalta, Evista, and Gemzar, but fail to communicate **any** risk information associated with the use of these drugs. In addition, the sponsored links for Evista and Gemzar inadequately communicate the drugs' indications. The sponsored link for Evista also fails to use the required established name. Thus, the sponsored links misbrand the drugs in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and FDA implementing regulations. See 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i), (ii) & (e)(6)(i).

**Background**

***Cymbalta***

According to its FDA-approved product labeling (PI), Cymbalta is indicated, among other things, for the acute and maintenance treatment of major depressive disorder (MDD).

Cymbalta is associated with a number of risks, as reflected in the Boxed Warning, Contraindications, Warnings and Precautions, and Adverse Reactions sections of its PI.

***Evista***

According to its FDA-approved PI, Evista is indicated for the following: the treatment and prevention of osteoporosis in postmenopausal women, the reduction in risk of invasive breast cancer in postmenopausal women with osteoporosis, and the reduction in risk of invasive breast cancer in postmenopausal women at high risk of invasive breast cancer. The PI includes important limitations of use for breast cancer risk reduction, including that Evista is

not indicated for the treatment of invasive breast cancer, the reduction of the risk of recurrence of breast cancer, or the reduction in the risk of noninvasive breast cancer.

Evista is associated with a number of risks, as reflected in the Boxed Warning, Contraindications, Warnings and Precautions, and Adverse Reactions sections of its PI.

### ***Gemzar***

According to its FDA-approved PI, Gemzar is indicated, among other things, in combination with cisplatin for the first-line treatment of patients with inoperable, locally advanced (Stage IIIA or IIIB), or metastatic (Stage IV) non-small cell lung cancer.

Gemzar is associated with a number of risks, as reflected in the Contraindication, Warnings, Precautions, and Adverse Reactions sections of its PI.

### **Omission of Risk Information**

Promotional materials, other than reminder pieces, which include the name of the drug product but do not include indications or other representations or suggestions relative to the drug product (see 21 CFR 200.200, 201.100(f), 202.1(e)(2)(i)), are required to disclose risk and other information about the drug. Such materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The sponsored links present the following claims:

- Cymbalta® (duloxetine HCl)  
[www.Cymbalta.com](http://www.Cymbalta.com) Learn about an SNRI for depression called Cymbalta® (duloxetine HCl).
- EVISTA - Official Site  
[www.EVISTA.com](http://www.EVISTA.com) Treats osteoporosis and proven to reduce invasive breast cancer risk.
- GEMZAR (gemcitabine HCl)  
[www.gemzar.com/hcp](http://www.gemzar.com/hcp) GEMZAR® is indicated to help treat 1st-line non-small cell lung cancer

These sponsored links make representations and/or suggestions about the efficacy of Cymbalta, Evista, and Gemzar, respectively, but fail to communicate **any** risk information. This omission of risk information is particularly concerning as two of the products, Cymbalta and Evista, have Boxed Warnings. For promotional materials to be truthful and non-misleading, they must contain risk information in each part as necessary to qualify any claims made about the drug.

By omitting the most serious and frequently occurring risks associated with the drugs promoted in the links above, the sponsored links misleadingly suggest that Cymbalta, Evista, and Gemzar are safer than has been demonstrated. We note that these sponsored links contain a link to the products' websites. However, this is insufficient to mitigate the

misleading omission of risk information from these promotional materials.

### **Inadequate Communication of Indication**

The sponsored links for Evista and Gemzar provide very brief statements of what the drugs are for; however, these statements are incomplete and misleading, suggesting that the drugs are useful in a broader range of conditions or patients than has been demonstrated by substantial evidence or substantial clinical experience.

Specifically, the sponsored link for Evista misleadingly broadens the indication for Evista by implying that all patients with osteoporosis are candidates for Evista therapy, and that Evista is proven to reduce the risk of invasive breast cancer in all patients ("Treats osteoporosis and proven to reduce invasive breast cancer risk."), when this is not the case. Rather, Evista is only indicated for the treatment and prevention of osteoporosis in postmenopausal women. Additionally, Evista's indication for the reduction in risk of invasive breast cancer is limited to two populations: postmenopausal women with osteoporosis and postmenopausal women at high risk of invasive breast cancer. Furthermore, there are several important limitations on Evista's use for breast cancer risk reduction in these populations, none of which are conveyed in the link.

The sponsored link for Gemzar misleadingly broadens the indication for Gemzar by implying that all patients with non-small cell lung cancer are candidates for Gemzar ("...indicated to help treat 1st-line non-small cell lung cancer"), when this is not the case. Additionally, the sponsored link fails to reveal that the drug is not indicated for monotherapy. Rather, Gemzar is only indicated in combination with cisplatin for first-line treatment of patients with inoperable, locally advanced or metastatic non-small cell lung cancer.

### **Failure to Use Required Established Name**

The sponsored link for Evista fails to present the full established name of the drug being promoted, despite the requirement to do so. See 21 CFR 201.10(g)(1) & 202.1(b)(1).

### **Conclusions and Requested Action**

For the reasons discussed above, the website sponsored links misbrand Cymbalta, Evista, and Gemzar, in violation of the Act and FDA regulations. See 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i), (ii) & (e)(6)(i).

DDMAC requests that Lilly immediately cease the dissemination of violative promotional materials for Cymbalta, Evista, and Gemzar, such as those described above. Please submit a written response to this letter on or before April 9, 2009, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) in use for these drugs as of the date of this letter, identifying which of these materials contain violations such as those described above, and explaining your plan for discontinuing use of such materials. Finally, we encourage you to review your promotional materials for the other prescription drug products that Lilly promotes in the United States and to discontinue or

revise any materials with the same or similar violations, and request that your response address this issue as well.

Please direct your response to the undersigned at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD, facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS # 17320 in addition to the NDA numbers. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Cymbalta, Evista, and Gemzar comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Michael Sauers  
Regulatory Review Officer  
Division of Drug Marketing,  
Advertising and Communications

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**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
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